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The Psychosis Prodrome: Biomarkers of the Glutamatergic System and Their Potential Role in Prediction and Treatment

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Abstract : The concept of the psychosis prodrome has allowed for the identification of adolescent and young adult patients who have a significantly elevated risk of developing schizophrenia spectrum disorders. A number of different interventions have been tested in order to prevent or delay progression of symptoms. To date, there has been no consistent meta-analytical evidence to support efficacy of antipsychotic treatment for patients in the prodromal state, and their use remains therefore inconclusive. Although antipsychotics may manage symptoms transiently, they have not been found to prevent or delay onset of psychotic disorders. Furthermore, pharmacological intervention in high-risk individuals remains controversial, because of the antipsychotic side effect profile in a population in which only about 20 to 35 percent will eventually convert to psychosis over a two-year period, with even after two years conversion rates not exceeding 30 to 40 percent. This general estimate is additionally problematic, in that it ignores the fact that there is significant variation in individual risk among clinical high-risk cases. The current lack of reliable tests for at-risk patients makes it difficult to justify individual treatment decisions. Preventive treatment should ideally be dictated by an individual's risk while minimizing potentially harmful medication exposure. This requires more accurate predictive assessments by using valid and accessible prognostic markers. The following will compare prediction and risk modification potential of behavioral biomarkers such as disturbances of basic sense of self and emotion awareness, neurocognitive biomarkers such as attention, working and declarative memory, and neurophysiological biomarkers such as glutamatergic abnormalities and NMDA receptor dysfunction. Identification of robust biomarkers could therefore not only provide more reliable means of psychosis prediction, but also help test and develop new clinical interventions targeted at the prodromal state.

Keywords : at-risk mental state, biomarkers, glutamatergic system, NMDA receptor, psychosis prodrome, schizophrenia
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